#4

PATENT
Attorney Docket No. 03495.0203

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Ute ROGNER, et al.	Group Art Unit: 1645
Serial No.: 09/847,665	Examiner: Not Assigned
Filed: May 3, 2001	
For: IDENTIFICATION OF NEURAL DEFECTS ASSOCIATED WITH THE *NUCLEOSOMAL ASSEMBLY PROTEIN* 112 GENE	

Commissioner for Patents and Trademarks
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to the examination of the above application, please amend this application as follows:

IN THE SPECIFICATION

Please replace the first full paragraph on page 6 with the following paragraph:

This invention also provides a recombinant chromosome comprising a polynucleotide containing a nucleotide sequence, wherein the sequence includes at least one modification of the *NAP1L2/Nap1l2*, wherein the modification is selected from a) substitution, b) deletion, c) frame-shift, d) aberrent insertion, e) altered epigenetic control, or f) site-directed mutagenesis that causes a loss of biological function in the *NAP1L2* gene.

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& DUNNER, L.L.P.
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Please insert the attach Sequence Listing (pages 1-5 and renumber the application accordingly.

IN THE CLAIMS:

Please cancel claims 4, 8, 11-14, 21, 23, 29-32, 42-44, and 50-53.

Please amend the following claims:

1. (AMENDED) A method for screening neural system defects in chromosomal material of a mammal, said method comprising:

(A) detecting a modification of a *NAP1L2* gene or a *Nap1l2* gene in the chromosomal material, wherein the modification is selected from a) substitution, b) deletion, c) frame-shift, d) aberrant insertion or e) altered epigenetic control that causes a loss of biological function in the *NAP1L2* gene or the *Nap1l2* gene; and

(B) correlating the modification of the gene with a potential for a neural system defect.

2. (AMENDED) The method of claim 1 wherein the mammal is a human.

3. (AMENDED) The method of claim 1, wherein the modification in the *NAP1L2* gene or the *Nap1l2* gene is detected by hybridization with a labeled probe.

5. (AMENDED) The method of claim 1, wherein the modification is detected by

(A) amplification of the chromosomal material using PCR;

(B) sequencing the chromosomal material to detect the modification of the nucleotide sequence; and

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(C) correlating the modification of the gene with a potential for neural system defects.

6. (AMENDED) A method for screening neural system defects in human or mouse biological material, said method comprising:

(A) detecting the absence, inappropriate, or modified expression of a *NAP1L2* gene product or a *Nap1l2* gene product using labeled antibodies to the gene product; and

(B) correlating the absence, inappropriate, or modified expression with a potential for neural system defects.

7. (AMENDED) The method of claim 6, wherein the antibodies are polyclonal or monoclonal.

9. (AMENDED) The method of claim 1, wherein the neural system defect results from at least one of a failure of neural tube closure, incomplete neural tube closure, inappropriate control of nucleosome activity in neurons, inappropriate control of the cell cycle in neurons, inappropriate differentiation of neurons, and inappropriate maintenance of neurons.

15. (AMENDED) A recombinant polynucleotide comprising a nucleotide sequence, wherein said sequence includes at least one modification of a *NAP1L2* gene or a *Nap1l2* gene, wherein the modification is selected from a) substitution, b) deletion, c) frameshift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *NAP1L2* gene or the *Nap1l2* gene.

17. (AMENDED) The polynucleotide of claim 15, wherein said polynucleotide is a chromosome or a part of a chromosome of a neural cell.

19. (AMENDED) The neural cell of claim 18, wherein the cell is derived from an immortal cell line, neuronal cell line, tumor derived cell line, embryonic stem cell, or wild type animal.

20. (AMENDED) The neural cell of claim 18, wherein the *NAP1L2* gene or the *Nap1l2* gene is under control of a neural-specific promoter, such as nestin, other neuronal members, and inducible promoters.

22. (AMENDED) The neural cell of claim 18, wherein the *NAP1L2* gene or the *Nap1l2* gene is modified, wherein said modification is a) substitution, b) deletion, c) frameshift, d) insertion, e) site-directed mutagenesis or f) naturally occurring mutation that causes a loss of biological function in the *NAP1L2* gene or *Nap1l2* gene.

24. (AMENDED) A polynucleotide comprising the promoter of a *Nap1l2* gene in SEQ ID NO:1, a polynucleotide hybridizing under stringent conditions with SEQ ID NO: 1, at least 20 nucleotides of SEQ ID NO: 1, the promoter of a *NAP1L2* gene in SEQ ID NO: 4, a polynucleotide hybridizing under stringent conditions with SEQ ID NO: 4, at least 20 nucleotides of SEQ ID NO: 4, SEQ ID NO: 6, a polynucleotide hybridizing under stringent conditions with SEQ ID NO:6, or at least 20 nucleotides of SEQ ID NO: 6.

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& DUNNER, L.L.P.
1300 I STREET, N. W.
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Genomic sequence *BPX* human (SEQ ID NO. 6)

1. acttaaaggaaaaatttatctataaactgacagaatttagaaataaatacaacaatatgtaaacagttttaatatctgtg
2. atagtaacaaattctttaaatctggaaaataatagtcacttaaaattttaaaaaattgttcaattaataaatgatccaag
3. ttagaaatatgaacaaaataaacctcaccaataattactatagagaggaaattttaattactgcaaagctttccatccta
4. taaatacattatcaaatagtttaaccatttctttaatgctgagatttagattatttccaattaactcaaaagcatcaagc
5. aaatgttatgatttctaagaataaacataactttccattttggcttttgtatatatgtatatttctaacggctgttaaag
6. ccagcattaagaaggagaagcagaaagtcagtattgggactggggttatttataagccaggcaactggttaattgtggtt
7. aattgtctggtatgtttactagtcacgtagttgtatacaccatactagtttttcatcacaggccctcattcgcccccact
8. gccatcggacttcctcctcctcccctcacaggaaatgtttcgagaatttttcaacctaaaatcatatagcttgtgaaaaa
9. taccgacaaacataatatagaatatttaaataactgacacgccacctaaagaccatcagtgctaattcctggtgttttta
10. atctttgaagcgtttgtttatcagctcttccaccatccacctctcccctccccaggtccccgatctaaaatcaaagagat
11. tgatttaggatgggtgggtgccttgtcttctctcattgttcgacattttagttacgttttctctgagctctctggaaagc
12. ataaaagtataatatctgttaaaagttggatgaatgaactaatgaacgcaatgggattccagaaaactctgcgggagatg
13. ggctagaggacgaggaggaggtggatgaatcagccatgttagagagcctgggaaggtgagcagagttgaaaacttgatag
14. atctaataatttactggctctgggtttgtcagtcactacattgcagcaaatgagattagaggatagttgtgggagggaag
15. gaggtgacgcagcaatctatttgcacctagaaattttaggcaagtgatagctgcgtaatcatactgcggcaccgttttct
16. tcttgcagcagtagctgcttgcggaggaggtctgcccactgcagctctctgcagtctccggctctctcctgcaggatcgg
17. tcaacgcagccgtcgccgccctctgcacccagcccaggtcgccactgcttcagtccggttctcaaagcctcagcaccatc
18. ttttatccccgagcagcctggatcgtcgttccctcagtccggacgccactgctaggtccgaccaccgccgcttctgatat
19. ttcggtgagtcttttcctgtggaggtttggtctcccgatctctgtggtagccaccttaggcgtgtacggtcctttgaaaa
20. ATGGCCGAGTCAGAGAACCGCAAGGAGCTGTCAGAATCCAGTCAAGAAGAGGCTGGTAATCAGATAATGGTGGAAGGGCT
21. CGGGGAACATCTGGAGCGCGGTGAAGATGCCGCTGCTGGGCTTGGAGACGATGGGAAGTGCGGTGAAGAAGCTGCCGCTG
22. GGCTTGGGGAAGAAGGGGAAAACGGTGAAGATACTGCTGCTGGGTCCGGGGAAGATGGGAAAAAAGGTGGCGATACTGAT
23. GAGGACTCAGAGGCAGACCGTCCAAAAGGACTTATCGGTTATGTTTTAGATACAGACTTTGTTGAAAGTCTACCTGTGAA
24. AGTTAAGTACCGTGTGTTAGCCCTTAAAAAGCTTCAAACTAGAGCGGCCAATTTAGAATCCAAATTCCTGAGGGAATTTC
25. ATGACATTGAAAGAAAGTTTGCTGAAATGTACCAACCCTTACTGGAAAAAAGACGTCAGATCATCAATGCAATCTATGAA
26. CCTACAGAAGAGGAATGTGAATATAAATCAGACTCTGAGGACTGTGATGATGAGGAAATGTGTCATGAAGAGATGTATGG
27. TAATGAGGAGGGTATGGTACATGAATATGTGGATGAGGACGATGGTTATGAGGACTATTATTATGATTATGCTGTGGAAG
28. AGGAGGAGGAGGAGGAGGAGGACGACATTGAGGCTACTGGAGAAGAGAATAAAGAAGAGGAGGATCCTAAGGGAATT
29. CCTGATTTTTGGCTAACTGTTTTAAAAAACGTTGATACACTCACTCCTTTGATTAAGAAATATGATGAGCCTATTCTGAA
30. GCTCCTGACAGATATTAAAGTTAAGCTTTCAGATCCTGGCGAGCCCCTCAGTTTCACACTAGAATTCACTTCAAACCCA
31. ATGAATATTTCAAAAATGaGTTGTTGACAAAGACCTATGTGCTGAAGTCAAAGCTAGCATATTATGATCCCCATCCCTAT
32. AGGGGAACTGCGATTGAGTATTCCACAGGCTGTGAGATAGATTGGAATGAAGGAAAGAATGTCACTTTGAAAACCATCAA
33. GAAGAAACAGAAACATCGGATCTGGGGAACAATCCGAACTGTAACTGAAGATTTTCCCAAGGATTCATTTTTCAATTTTT
34. TCTCTCCTCATGGAATCACCTCAAATGGAAGGGATGGAAATGATGATTTTTTACTTGGTCACAATTTACGTACTTACATA
35. ATTCCAAGATCAGTATTATTTTTCTCAGGTGATGCACTGGAATCTCAGCAGGAGGGGGTAGTTAGAGAAGTTAATGATGC
36. AATTTATGACAAAATTATTTATGATAATTGGATGGCTGCAATTGAGGAAGTTAAAGCTTGTTGCAAAAACCTTGAGGCAT
37. TAGTAGAAGACATTGATCGTTAGAGCagagtatacatggccctgaaattaactgccctagatatagttactcaaggtata
38. agaagccttgtgttctgtattttgctttgtagtgttagttaaaacatatgtttcaaaaatataagaaaagttcaaaaact
39. aattaatttgaccttgagttttagtagtagaatgttttcaagaaatgtacactgtggtaaatgatttaaaacactagtat
40. agtgttgtgtagcttaatccttctgaagtctttttgtcatgtagctattaatctgtggctatgaaatgatcagaaatgct
41. aagtgagatcaatatttgtttgcaaaaaaaatcttgggaaacaacccaagggttttcgctgttgttgtttttctttttct
42. atttttgtttacttagtcctttagctagtggatttaattttgttgtgcctgcttcattttgcaataacaatgcagtagaa
43. tttaaaacttggatgcttaagaggcctgcatatagataagaatttcaggcaaaactacatttattgttaataacagcttg
44. ttcataggctcttgtatttttatgtaactgtgataaataatgaaaacttagttatattgaggttattgtttgtcggtgaag
45. tgttagtcacagtattttcaaaagtttgcacatattgttctgtgtaattgtgtaagccataattacagtgtttaattctc
46. ttttcctattacatcattcattgaaagtgatcactttaccattttgaaaagatatttcgtgttctttcactgcaaaataa
47. aaagaataaaaatttcaga

26. (AMENDED) A method of making a recombinant neural cell comprising:

(A) modifying a *NAP1L2* gene or a *Nap1l2* gene or a promoter of the *NAP1L2* gene or a promoter of the *Nap1l2* gene in a neural cell, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, and d) insertion that causes a loss of biological function in the gene; and

(B) selecting modified cells.

27. (AMENDED) A method of screening for therapeutic compounds comprising:

(A) introducing a compound to be screened to the cell of claim 18; and

(B) correlating a change in the proliferation of the cells with the activity of the compound.

28. (AMENDED) A method of screening for therapeutic compounds comprising:

(A) introducing a compound to be screened to a transgenic knockout animal containing the human *NAP1L2* gene in its chromosomes; and

(B) correlating a change in the development and maturation of the transgenic knockout animal nervous system with the activity of the compound.

33. (AMENDED) A vector containing the nucleic acid molecule of claim 24.

34. (AMENDED) A recombinant neural cell comprising a vector, wherein the vector comprises the *Nap1l2* gene or the *NAP1L2* gene.

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35. (AMENDED) The neural cell of claim 34, wherein the *Nap1l2* gene or the *NAP1L2* gene is under the control of a neural-specific promoter, such as nestin or other neuronal genes or inducible promoters.

36. (AMENDED) A recombinant neural cell of claim 35, wherein the *Nap1l2* gene or the *NAP1L2* gene of the native cell is modified, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *Nap1l2* gene or the *NAP1L2* gene.

37. (AMENDED) A method of screening for therapeutic compounds in a cell comprising the nucleotide of claim 24, wherein the method comprises:

(A) introducing to the cell a compound to be screened; and

(B) correlating a change in the proliferation of the cell with activity of the compound.

39. (AMENDED) A method of increasing the expression of *NAP1L2* gene in tumoral human neural cells or for decreasing the expression of *NAP1L2* gene in human neural cells afflicted by a degenerating disease, comprising administering the therapeutic compounds of claim 27 to achieve an increase in expression of *NAP1L2* gene in tumoral human neural cells or a decrease in expression of *NAP1L2* gene in human neural cells afflicted by a degenerating disease.

41. (AMENDED) The plasmid deposited at C.N.C.M. under the Accession Number I-2463, I-2464, I-2465, or I-2466.

45. (AMENDED) A polynucleotide comprising the sequence SEQ ID NO: 6.

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46. (AMENDED) The polynucleotide of claim 24, wherein said polynucleotide further comprises a heterologous amino acid sequence coding for a heterologous polypeptide under the control of the *NAP1L2* promoter or the *Nap1l2* promoter.

Please add the following new claims:

54. (NEW) The method of claim 1, wherein the mammal is a mouse.

55. (NEW) The method of claim 6, wherein the neural system defect results from at least one of a failure of neural tube closure, incomplete neural tube closure, inappropriate control of nucleosome activity in neurons, inappropriate control of the cell cycle in neurons, inappropriate differentiation of neurons, and inappropriate maintenance of neurons.

56. (NEW) The polynucleotide of claim 16, wherein said polynucleotide is a chromosome or a part of a chromosome of a neural cell.

57. (NEW) A neural cell comprising the polynucleotide of claim 56.

58. (NEW) The neural cell of claim 57, wherein the cell is derived from an immortal cell line, neuronal cell line, tumor derived cell line, embryonic stem cell, or wild type animal.

59. (NEW) The neural cell of claim 57, wherein the *NAP1L2* gene or the *Nap1l2* gene is under control of a neural-specific promoter, such as nestin, other neuronal members, and inducible promoters.

60. (NEW) The neural cell of claim 57, wherein the *NAPIL2* gene or the *Nap1l2* gene is modified, wherein said modification is a) substitution, b) deletion, c) frameshift,

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d) insertion, e) site-directed mutagenesis or f) naturally occurring mutation that causes a loss of biological function in the *NAPIL2* gene or *Nap1l2* gene.

61. (NEW) The neural cell of claim 57, wherein the *NAP1L2* gene is modified, wherein the modification is selected from a) substitution, b) deletion, c) frameshift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *NAP1L2* gene.

REMARKS

Entry of this Amendment prior to examination is respectfully requested.

The amendment to page 6 of the specification does not add new matter because it merely corrects a typographical error. A "NapsII" gene is not the focus of the invention, and is not recited anywhere else in the specification. Instead, the term "NapsII" is a typographical error in the term "*Nap1l2*," a term which is recited numerous other times in the specification. The error in the term "NapsII" is also clear because it is used on page 6 in conjunction with the term "*NAP1L2*", which is the human homologue of the mouse *Nap1l2* gene.

New claims 54-61 and amended claims 1-3, 5-7, 9, 15, 17, 19, 20, 22, 24, 26, 27, 28, 33-37, 39, 41, 45 and 46 do not add new matter to the specification, but were derived from the original claims and were changed to conform to United States patent practice.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

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NNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
ASHINGTON, DC 20005
202-408-4000

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 12, 2001

By: _____
Kenneth J. Meyers
Reg. No. Reg. No. 25,146

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NNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
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Appendix to the Amendment of October 12, 2001

IN THE SPECIFICATION

Please replace the first full paragraph on page 6 with the following paragraph:

This invention also provides a recombinant chromosome comprising a polynucleotide containing a nucleotide sequence, wherein the sequence includes at least one modification of the *NAP1L2*/[NapsII] *Nap1l2* gene, wherein the modification is selected from a) substitution, b) deletion, c) frame-shift, d) aberrent insertion, e) altered epigenetic control, or f) site-directed mutagenesis that causes a loss of biological function in the *NAP1L2* gene.

IN THE CLAIMS

Please amend the following claims:

1. (AMENDED) A method for screening neural system defects in chromosomal material of a mammal, said method comprising:

[(A) providing chromosomal material from said human;]

[(B)](A) detecting a modification of [the] a *NAP1L2* gene or a *Nap1l2* gene in the chromosomal material, wherein [said]the modification is selected from a) substitution, b) deletion, c) frame-shift, d) aberrant insertion [aberent]or e) altered epigenetic control[;] that causes a loss of biological function in the *NAP1L2* gene or the *Nap1l2* gene; and

[(C)](B) correlating the modification of [said]the gene with a potential for a neural system defect.

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2. (AMENDED) [A]The method [according to]of claim 1[where the said screening of neural system defects concerns a human being] wherein the mammal is a human.

3. (AMENDED) The method of claim 1, wherein [said] the modification in the *NAP1L2* gene or the *Nap1l2* gene is detected by hybridization with a labeled probe.

5. (AMENDED) [A]The method of claim 1, wherein [said] the modification is detected by

(A) amplification of the chromosomal material using PCR;

(B) sequencing [said] the chromosomal material to detect the modification of the nucleotide sequence; and

(C) correlating the modification of [said] the gene with a potential for neural system defects.

6. (AMENDED) A method for screening neural system defects in [a]human or mouse biological material, said method comprising:

[(A) providing biological material from said human;]

[(B)](A) detecting the absence, inappropriate, or modified expression of a *NAP1L2* gene product or a *Nap1l2* gene product using labeled antibodies to [said]the gene product; and

[(C)](B) correlating [said]the absence, inappropriate, or modified expression with a potential for neural system defects.

7. (AMENDED) The method of claim [5]6, wherein the [said]antibodies are polyclonal or monoclonal.

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9. (AMENDED) [A]The method of [any one of claims]claim 1[to 8], wherein the neural system defect results from at least one of a failure of neural tube closure, [or]incomplete neural tube closure, inappropriate control of nucleosome activity in neurons, inappropriate control of the cell cycle in neurons, inappropriate differentiation of neurons, and inappropriate maintenance of neurons.

15. (AMENDED) A recombinant polynucleotide comprising a nucleotide sequence, wherein said sequence includes at least one modification of [the NAP1L2] a *NAP1L2* gene or a *Nap1l2* gene, wherein [said] the modification is selected from a) substitution, b) deletion, c) frameshift, d) insertion, or e) site-directed [mutagensis]mutagenesis that causes a loss of biological function in the *NAP1L2* gene or the *Nap1l2* gene.

17. (AMENDED) The polynucleotide of claim 15 [or 16], wherein said polynucleotide is a chromosome or a part of [it] a chromosome of a neural cell.

19. (AMENDED) The neural cell of claim 18, wherein the cell is derived from an immortal cell line, [such as embryonic stem cells], neuronal cell line, [or] tumor derived cell line, embryonic stem cell, or wild type animal.

20. (AMENDED) The neural cell of claim 18, wherein the *NAP1L2* gene or the *Nap1l2* gene is under control of a neural-specific promoter, such as nestin, other neuronal members, and inducible promoters.

22. (AMENDED) The neural cell of claim 18, [20, or 21,] wherein the *NAP1L2* gene or the *Nap1l2* gene is modified, wherein said modification is [selected from] a) substitution, b) deletion, c) frameshift, d) insertion, [or] e) site-directed mutagenesis or f)

naturally occurring mutation that causes a loss of biological function in the *NAP1L2* gene or *Nap1l2* gene.

24. (AMENDED) A polynucleotide comprising the promoter of a *Nap1l2* gene in SEQ ID NO:1, a polynucleotide hybridizing under stringent conditions with SEQ ID NO: 1, at least 20 nucleotides of SEQ ID NO: 1, the promoter of [the] a *NAP1L2* gene in SEQ ID NO: 4, [or] a polynucleotide hybridizing under stringent conditions with SEQ ID NO: 4, [or] at least 20 nucleotides of [said] SEQ ID NO: 4, SEQ ID NO: 6, a polynucleotide hybridizing under stringent conditions with SEQ ID NO:6, or at least 20 nucleotides of SEQ ID NO: 6.

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FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
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Genomic sequence *BPX* human (SEQ ID NO. 6)

1. acttaaaggaaaaatttatctataaactgacagaatttagaaataaatacaacaatatgtaaacagttttaatatctgtg
2. atagtaacaaattctttaaatctggaaaataatagtcacttaaaatttaaaaaattgttcaattaataaatgatccaag
3. ttagaaatatgaacaaaataaacctcaccaataattactatagaggaaatttttaattactgcaaagctttccatccta
4. taaatacattatcaaatagtttaaccatttctttaatgctgagatttagattatttccaattaactcaaaagcatcaagc
5. aaatgttatgatttctaagaataaacataactttccattttggcttttgtatatatgtatatttctaacggctgttaaag
6. ccagcattaagaaggagaagcagaaagtcagtattgggactggggttatttataagccaggcaactggttaattgtggtt
7. aattgtctggtatgtttactagtcacgtagttgtatacaccatactagtttttcatcacaggccctcattcgccccact
8. gccatcggacttcctcctcctcccctcacaggaaatgtttcgagaatttttcaacctaaaatcatatagcttgtgaaaaa
9. taccgacaaacataatatagaatatttaaataactgacacgccacctaaagaccatcagtgctaattcctggtgttttta
10. atctttgaagcgtttgtttatcagctcttccaccatccacctctcccctccccaggtccccgatctaaaatcaaagagat
11. tgatttaggatgggtgggtgccttgtcttctctcattgttcgacattttagttacgttttcctgagctctctggaaagc
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14. atctaataatttactggctctgggtttgtcagtcactacattgcagcaaatgagattagagcatagttgtgggagggaag
15. gaggtgacgcagcaatctatttgcacctagaaattttaggcaagtgatagctgcgtaatcatactgcggcaccgtttttt
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17. tcaacgcagccgtcgccgccctctgcacccagcccaggtcgccactgcttcagtccggttctcaaagcctcagcaccatc
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19. ttcggtgagtcttttcctgtggaggtttggtctcccgatctctgtggtagccaccttaggcgtgtacggtcctttgaaaa
20. ATGGCCGAGTCAGAGAACCGCAAGGAGCTGTCAGAATCCAGTCAAGAAGAGGCTGGTAATCAGATAATGGTGGAAGGGCT
21. CGGGGAACATCTGGAGCGCGGTGAAGATGCCGCTGCTGGGCTTGGAGACGATGGGAAGTGCGGTGAAGAAGCTGCCGCTG
22. GGCTTGGGGAAGAAGGGGAAAACGGTGAAGATACTGCTGCTGGGTCCGGGGAAGATGGGAAAAAAGGTGGCGATACTGAT
23. GAGGACTCAGAGGCAGACCGTCCAAAAGGACTTATCGGTTATGTTTTAGATACAGACTTTGTTGAAAGTCTACCTGTGAA
24. AGTTAAGTACCGTGTGTTAGCCCTTAAAAAGCTTCAAACTAGAGCGGCCAATTTAGAATCCAAATTCCTGAGGGAATTTC
25. ATGACATTGAAAGAAAGTTTGCTGAAATGTACCAACCCTTACTGGAAAAAAGACGTCAGATCATCAATGCAATCTATGAA
26. CCTACAGAAGAGGAATGTGAATATAAATCAGACTCTGAGGACTGTGATGATGAGGAAATGTGTCATGAAGAGATGTATGG
27. TAATGAGGAGGGTATGGTACATGAATATGTGGATGAGGACGATGGTTATGAGGACTATTATTATGATTATGCTGTGGAAG
28. AGGAGGAGGAGGAGGAGGAGGACGACATTGAGGCTACTGGAGAAGAGAATAAAGAAGAGGAGGATCCTAAGGGAATT
29. CCTGATTTTTGGCTAACTGTTTTAAAAAACGTTGATACACTCACTCCTTTGATTAAGAAATATGATGAGCCTATTCTGAA
30. GCTCCTGACAGATATTAAAGTTAAGCTTTCAGATCCTGGCGAGCCCCTCAGTTTCACACTAGAATTTCACTTCAAACCCA
31. ATGAATATTTCAAAAATGaGTTGTTGACAAAGACCTATGTGCTGAAGTCAAAGCTAGCATATTATGATCCCCATCCCTAT
32. AGGGGAACTGCGATTGAGTATTCCACAGGCTGTGAGATAGATTGGAATGAAGGAAAGAATGTCACTTTGAAAACCATCAA
33. GAAGAAACAGAAACATCGGATCTGGGGAACAATCCGAACTGTAACTGAAGATTTTCCCAAGGATTCATTTTTCAATTTTT
34. TCTCTCCTCATGGAATCACCTCAAATGGAAGGGATGGAAATGATGATTTTTTACTTGGICACAATTTACGTACTTACATA
35. ATTCCAAGATCAGTATTATTTTTCTCAGGTGATGCACTGGAATCTCAGCAGGAGGGGGTAGTTAGAGAAGTTAATGATGC
36. AATTTATGACAAAATTATTTATGATAATTGGATGGCTGCAATTGAGGAAGTTAAAGCTTGTTGCAAAAACCTTGAGGCAT
37. TAGTAGAAGACATTGATCGTTAGAGCagagtatacatggccctgaaattaactgccctagatatagttactcaaggtata
38. agaagccttgtgttctgtattttgctttgtagtgttagttaaaacatatgtttcaaaaatataagaaaagttcaaaaact
39. aattaatttgaccttgagttttagtagtagaatgttttcaagaaatgtacactgtggtaaatgatttaaaacactagtat
40. agtgttgtgtagcttaatccttctgaagtctttttgtcatgtagctattaatctgtggctatgaaatgatcagaaatgct
41. aagtgagatcaatatttgtttggaaaaaaaatcttgggaaacaacccaagggttttcgctgttgttgtttttctttttct
42. atttttgtttacttagtcctttagctagtggatttaattttgttgtgcctgcttcattttgcaataacaatgcagtagaa
43. tttaaaacttggatgcttaagaggcctgcatatagataagaatttcaggcaaaactacatttattgttaataacagcttg
44. ttcataggctcttgtattttatgtaactgtgataaataatgaaaacttagttatattgaggttattgtttgtcggtgaag
45. tgttagtcacagtattttcaaaagtttgcacatattgttctgtgtaattgtgtaagccataattacagtgtttaattctc
46. ttttcctattacatcattcattgaaagtgatcactttaccattttgaaaagatatttcgtgttctttcactgcaaaataa
47. aaagaataaaaatttcaga

26. (AMENDED) A method of making a recombinant neural cell comprising:

[(A) providing a neural cell;]

[(B)] (A) modifying a *NAP1L2* gene or a *Nap1l2* gene or [the] a promoter of the *NAP1L2* gene or a promoter of the *Nap1l2* gene in [the] a neural cell, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, and d) insertion that causes a loss of biological function in the gene; and

[(C)] (B) selecting modified cells.

27. (AMENDED) A method of screening for therapeutic compounds comprising:

[(A) providing a cell of any one of claims 18 to 23;]

[(B)] (A) introducing a compound to be screened to the cell of claim 18 [a compound to be screened]; and

[(C)] (B) correlating a change in the proliferation of the cells with the activity of the compound.

28. (AMENDED) A method of screening for therapeutic compounds comprising:

[(A) providing a transgenic knockout animal containing the human *NAP1L2* gene in its chromosomes.]

[(B)] (A) introducing a compound to be screened to [the] a transgenic knockout animal containing the human *NAP1L2* gene in its chromosomes [a compound to be screened]; and

[(C)] (B) correlating a change in the development and maturation of the transgenic knockout animal nervous system with the activity of the compound.

33. (AMENDED) A vector containing the nucleic acid molecule of claim [32] 24.

34. (AMENDED) A recombinant neural cell comprising a vector [comprising] wherein the vector comprises the *Nap1l2* gene or the *NAP1L2* gene.

35. (AMENDED) The neural cell of claim 34, wherein the *Nap1l2* gene or the *NAP1L2* gene is under the control of a neural-specific promoter, such as nestin or other neuronal genes or inducible promoters.

36. (AMENDED) A recombinant neural cell of claim 35, wherein the *Nap1l2* gene or the *NAP1L2* gene of the native cell is modified, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *Nap1l2* gene or the *NAP1L2* gene.

37. (AMENDED) A method of screening for therapeutic compounds in a cell comprising the nucleotide of claim 24, wherein the method comprises:

[(A) providing a cell containing a polynucleotide according to claim 32;]

[(B)] (A) introducing to the cell a compound to be screened; and

[(C)] (B) correlating a change in the proliferation of the cell with activity of the compound.

39. (AMENDED) [Use of therapeutic compounds obtained by the method according to claim 27 for] A method of increasing the expression of *NAP1L2* gene in

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1300 I STREET, N. W.
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tumoral human neural cells or for decreasing the expression of *NAP1L2* gene in human neural cells afflicted by a degenerating disease, comprising administering the therapeutic compounds of claim 27 to achieve an increase in expression of *NAP1L2* gene in tumoral human neural cells or a decrease in expression of *NAP1L2* gene in human neural cells afflicted by a degenerating disease.

41. (AMENDED) [A] The plasmid [consisting in the deposit made at] deposited at C.N.C.M. under the Accession Number I-2463, I-2464, I-2465, or I-2466.

45. (AMENDED) A polynucleotide [containing] comprising the sequence SEQ ID NO: 6.

46. (AMENDED) The polynucleotide of claim 24, wherein said polynucleotide further comprises [an] a heterologous amino acid sequence coding for [an] a heterologous polypeptide under the control of the *NAP1L2* promoter or the *Nap1l2* promoter.

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1300 I STREET, N. W.
VASHINGTON, DC 20005
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